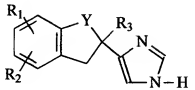
REMARKS

This application has been reviewed in light of the Office Action dated July 8, 2010. Claims 1, 3 and 6-18 are presented for examination, of which claim 1 is in independent form. Claim 1 has been amended to better define the intended invention and to incorporate the subject matter of cancelled claims 4 and 5. As such, claims 4 and 5 have been cancelled without prejudice or disclaimer of subject matter. Claims 6 and 10 have been amended as to matters of form only to correct claim dependency. Favorable reconsideration is requested.

Claims 1, 3-4, 12-15 and 17-18 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,292,887 (Karjalainen). Claims 1, 3 and 12-18 have been rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Karjalainen. Applicants respectfully traverse the rejections.

Prior to addressing the grounds of rejection, Applicants wish to briefly review certain features and advantages of the presently claimed invention. The invention is directed, in pertinent part, to a fast-dispersing, solid dosage form formulated to disintegrate within 10 seconds of being placed in the oral cavity comprising, as an active ingredient, a substituted imidazole derivative of general formula (I),



(I)

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so as to promote pre-gastric absorption of the active ingredient. The invention relates to an improved formulation comprising a substituted imidazole derivative and one or more matrix forming agents comprising one or more of gelatin and a cyclic sugar. In the past, substituted imidazoles have shown disadvantages, such as quick decomposition in the stomach (which

lowers the effectiveness of the composition) and transient adverse reactions (such as white spots and numbness). Page 1, line 18 through page 2, line 10 of the subject specification as filed. The inventors of the subject invention discovered that if the compounds of formula (I) are administered in a fast-dispersing solid dosage form, so that they are absorbed through the oral mucosal membrane, or otherwise pre-gastrically, many of these disadvantages can be avoided and bioavailability improved. See page 2, lines 13-16.

As demonstrated by the comparative examples in the subject specification as filed, the fast-dispersing, solid dosage form of the subject invention achieves unexpectedly superior properties over a buccal spray and over oral administration of a solution containing an imidazole derivative. As demonstrated by Comparison 1, "the bioavailability of non-metabolised fipamezole by oral route is unsatisfactory" while fipamezole was rapidly absorbed in a dose-dependent manner with the buccal spray. Page 11, line 10 through page 12, line 6. Comparison 2 demonstrates the rapid absorption of fipamezole in the fast-dispersing, solid dosage form via pre-gastric absorption (buccal cavity). Comparison 3 demonstrates that the fast-dispersing, solid dosage of the subject invention offers advantages in patient compliance because patients do not show signs of buccal erythema and whitening with its use, unlike with use of the buccal spray. Page 14, line 10-15. Accordingly, with the fast-dispersing, solid dosage of the subject invention, rapid absorption and increased patient safety is possible over other forms of oral administration. Therefore, these unexpectedly superior characteristics rebut a presumption of obviousness of the fast-dispersing, solid dosage form of the present invention.

Karjalainen is directed to substituted imidazole derivatives. As disclosed therein, the compounds "may be administered orally, parenterally or intravenously." Karjalainen fails to disclose or suggest use of the imidazole derivatives in a fast-dispersing, solid dosage form, the

benefits of pre-gastric absorption of the active ingredient, or the potential to use the compound in a form which disintegrates within 10 seconds of being placed in the oral cavity. Simply indicating that the compound may be administered orally does not disclose, nor in any way suggest, the benefits of administering the drug so that it is rapidly absorbed pre-gastrically. As explained above and shown at page 12, lines 4-9 of the subject specification, oral dosing of fipamezole, an imidazole derivative, shows unsatisfactory bioavailability. Since Karjalainen fails to recognize the differences between general oral administration and administration by fast-dispersing, solid dosage form, it further fails to realize that this leads to improved characteristics, including bioavailability.

On page 3 of the Office Action, the Examiner alleges that "inherently the solid drug of Karjalainen would provide pre-gastric absorption of the active ingredient."

"To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill...'" MPEP § 2112 *citing In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Further, *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) states that "[i]n relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." (Emphasis in original.)

The Examiner has not presented a basis in fact or technical reason to reasonably support the determination that the characteristic alleged as inherent necessarily flows from the teachings of Karjalainen. Karjalainen does not teach or suggest the use of a fast-dispersing, solid dosage form. The general statement that the formulation may be administered orally,

parenterally or intravenously and may be solid or liquid does not lead one of ordinary skill in the art to make a dosage form that will disintegrate within 10 seconds of being placed in the oral cavity. The dosage form of Karjalainen is likely a swallowable, solid or a slow-dissolving, solid, chewable dosage form.

In addition, Karjaleinen fails to teach or suggest the fast-dispersing, solid dosage form further containing one or more matrix forming agents comprising one or more of gelatin and a cyclic sugar. In sum, since Karjalainen fails to teach or suggest all of the features of the presently claimed invention, Applicants request withdrawal of the § 102 and § 103 rejections in view of Karjaleinen.

Claims 1, 4-6 and 8 were also rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Karjalainen, in view of U.S. Patent No. 4,968,692 (Linnoila); claims 1-6 and 8-11 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Karjalainen, in view of U.S. Patent No. 6,316,027 (Johnson); and claims 1-18 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Karjalainen, in view of U.S. Patent No. 6,709,669 (Murray). Applicants respectfully traverse the rejections.

For all of the reasons set forth above, Karjalainen fails to disclose or suggest several key features of the present invention. Linnoila, Johnson and Murray fail to remedy these deficiencies of Karjalainen. Linnoila is deficient in that there is simply no teaching or suggestion of a fast-dispersing, solid dosage form for pre-gastric absorption of the active ingredient, which disintegrates within 10 seconds of being placed in the oral cavity. Johnson and Murray are also deficient insofar as they provide no reasonable expectation of success that the fast-dispersing dosage forms disclosed therein could be used for the presently claimed substituted imidazole derivatives. These references also fail to appreciate the unexpectedly superior results that may be

achieved by formulating an imidazole derivative in a fast-dispersing, solid dosage form, as explained above, over both oral administration of a solution and over a buccal spray.

In sum, Applicants submit that the present invention is not rendered obvious by Karjalainen, Linnoila, Johnson or Murray, whether considered separately or in any permissible combination. There is simply no disclosure or suggestion in the cited art of a presently claimed fast-dispersing, solid dosage form comprising, as an active ingredient, a substituted imidazole derivative, which promotes pre-gastric absorption and disintegrates in 1-10 seconds, and one or more matrix forming agents comprising one or more of gelatin and a cyclic sugar. For at least these reasons, Applicants respectfully request withdrawal of the §103 rejections.

Claims 1-18 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over claims 23 and 25-33 of co-pending U.S. Patent Application No. 10/534,091. Applicants submit that the applications are directed to non-obvious variations and respectfully request withdrawal of the rejection.

As amended herein, claim 1 is directed to a fast-dispersing, solid dosage form, further containing one or more matrix forming agents comprising one or more of gelatin and a cyclic sugar. This dosage form is specifically utilized to impart quick release characteristics to the subject invention. Since the claims of U.S. Patent Application No. 10/534,091 fail to recite or suggest this limitation, the subject invention is not rendered obvious therefrom. Withdrawal of the provisional double-patenting rejection is respectfully requested.

In view of the foregoing amendments and remarks, Applicants respectfully request favorable reconsideration and early passage to issue of the present application.

Applicants' undersigned attorney may be reached in our New York Office by telephone at (212) 218-2100. All correspondence should continue to be directed to our address listed below.

Respectfully submitted,

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